



Year: 2011

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Abstract: **BACKGROUND:** Moyamoya disease (MMD) is an idiopathic progressive arteriopathy affecting the proximal intracranial vasculature. To date only 4 case reports on intracranial angioplasty or stenting as treatment of this disease exist. We present 5 adult patients with MMD who failed angioplasty and/or stenting who remained symptomatic despite endovascular treatment or presented with recurrent symptoms and recurrence of stenosis/occlusion on angiography requiring subsequent extracranial-intracranial revascularization. **METHODS:** Five adult MMD patients who underwent endovascular treatment with angioplasty or stenting were referred for further evaluation and treatment from outside hospitals. Data were collected from clinical referral notes and angiograms or reports. All patients underwent repeat 6-vessel cerebral angiography to assess the extent of disease and results of prior endovascular treatment. **RESULTS:** Six endovascular procedures were performed in all 5 patients. Internal carotid artery (ICA) balloon angioplasty and Wingspan stenting was performed in 2 patients (3 arteries). One patient had ICA-M1 angioplasty without stenting. Two patients had M1 angioplasty and Wingspan stenting. All patients developed repeat transient ischemic attacks following treatment attributable to the vascular territories of endovascular treatment. Repeat endovascular treatment was performed in 3 patients at a mean of 4 months (range = 2-6). Two went on to a third endovascular treatment due to progression of disease in the angioplastied/stented vessel. The average time of symptom recurrence after initial endovascular therapy was 1.8 months (0-4 months). Follow-up angiography when referred to our institution demonstrated 70-90% instant restenosis of the stented vessel in 3 and occlusion in 1 patient. Due to persistence of symptoms cerebral revascularization was performed in all patients. **CONCLUSION:** MMD is a progressive angiopathy. Angioplasty and stenting may temporarily improve the cerebral blood flow and decrease cerebral ischemic events but do not appear to be durable nor provide long-term prevention against future ischemic events.

DOI: <https://doi.org/10.1159/000320253>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-45251>

Journal Article

Published Version

Originally published at:

Khan, N; Dodd, R; Marks, M P; Bell-Stephens, T; Vavao, J; Steinberg, G K (2011). Failure of primary percutaneous angioplasty and stenting in the prevention of ischemia in moyamoya angiopathy. *Cerebrovascular Diseases*, 31(2):147-153.

DOI: <https://doi.org/10.1159/000320253>

Failure of Primary Percutaneous Angioplasty and Stenting in the Prevention of Ischemia in Moyamoya Angiopathy

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Key Words

Angioplasty • Moyamoya • Wingspan stent

Abstract

Background: Moyamoya disease (MMD) is an idiopathic progressive arteriopathy affecting the proximal intracranial vasculature. To date only 4 case reports on intracranial angioplasty or stenting as treatment of this disease exist. We present 5 adult patients with MMD who failed angioplasty and/or stenting who remained symptomatic despite endovascular treatment or presented with recurrent symptoms and recurrence of stenosis/occlusion on angiography requiring subsequent extracranial-intracranial revascularization.

Methods: Five adult MMD patients who underwent endovascular treatment with angioplasty or stenting were referred for further evaluation and treatment from outside hospitals. Data were collected from clinical referral notes and angiograms or reports. All patients underwent repeat 6-vessel cerebral angiography to assess the extent of disease and results of prior endovascular treatment. **Results:** Six endovascular procedures were performed in all 5 patients. Internal carotid artery (ICA) balloon angioplasty and Wingspan stenting was performed in 2 patients (3 arteries). One patient had ICA-M1 angioplasty without stenting. Two patients had M1 angioplasty and Wingspan stenting. All patients devel-

oped repeat transient ischemic attacks following treatment attributable to the vascular territories of endovascular treatment. Repeat endovascular treatment was performed in 3 patients at a mean of 4 months (range = 2–6). Two went on to a third endovascular treatment due to progression of disease in the angioplastied/stented vessel. The average time of symptom recurrence after initial endovascular therapy was 1.8 months (0–4 months). Follow-up angiography when referred to our institution demonstrated 70–90% in-stent restenosis of the stented vessel in 3 and occlusion in 1 patient. Due to persistence of symptoms cerebral revascularization was performed in all patients. **Conclusion:** MMD is a progressive angiopathy. Angioplasty and stenting may temporarily improve the cerebral blood flow and decrease cerebral ischemic events but do not appear to be durable nor provide long-term prevention against future ischemic events.

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Introduction

Moyamoya disease (MMD) is an idiopathic progressive angiopathy typically seen in young adults involving the internal carotid artery (ICA) and adjacent middle (M1 segment) and anterior (A1 segment) cerebral arteries [1–4]. Segmental changes often begin with focal irregu-

Table 1. Moyamoya patients with failed angioplasty and stenting

	Age/ sex	Initial presenting symptoms	Stenoses	Endovascular treatment	Repeat endovascular treatment
1	38/F	headaches, seizure, bilateral watershed infarcts	70% right supraclinoid ICA stenosis 80% left supraclinoid ICA stenosis	ICA-M1 angioplasty and Wingspan stent – no residual stenosis ICA-M1 angioplasty, Wingspan stent – no significant residual stenosis	yes/angioplasty of instent stenosis yes/angioplasty of instent stenosis
2	39/M	headaches, visual disturbances, right homonymous hemianopsia, PCA infarct	70% left supraclinoid ICA-proximal M1 stenosis	ICA-M1 angioplasty – no residual stenosis	no
3	19/F	TIA's: dysarthria, left-sided numbness	right supraclinoid ICA occlusion, >70% left supraclinoid ICA stenosis	ICA angioplasty and Wingspan stent – 30% residual stenosis	no
4	32/F	right hemiparesis, aphasia	90% left M1 stenosis	M1 angioplasty and Wingspan stent – no residual stenosis	yes/second Wingspan inside the first stent for instent stenosis M1 angioplasty for recurrence of instent stenosis
5	37/F	right hemiparesis, aphasia	60–70% left M1 stenosis	M1 angioplasty and Wingspan stent – no residual stenosis	yes/angioplasty of instent stenosis yes/angioplasty of instent stenosis

STA-MCA = Superficial temporal artery to middle cerebral artery; PCA = posterior cerebral artery.

larities isolated to the ICA, which later progress to complete occlusion and development of staged collaterals along the circle of Willis.

No known medical therapy exists to reverse these arterial changes, which can result in progressive ischemia or hemorrhage. Endovascular percutaneous balloon angioplasty and/or stenting have emerged as viable alternatives to surgery for intracranial atherosclerotic disease. The success and durability of such techniques for stroke prevention in MMD is unclear. To date there have been 4 published case reports of endovascular treatment for MMD [5–8].

Methods

Five MMD patients, with an average age of 33 years (range = 19–39 years; M:F = 1:4), underwent endovascular treatment and were subsequently referred to our center for further evaluation and treatment due to recurrent symptoms. Data were collected

from available clinical referral notes and from outside angiograms or reports. All patients were seen and examined in our outpatient clinic. We performed a repeat 6-vessel cerebral angiography to evaluate the extent of disease and results of prior endovascular treatment in all patients.

Results

Table 1 summarizes the lesion locations, symptoms, endovascular treatment and outcomes for the patients. The 5 patients underwent treatment of 6 lesions. Four ICA or combined ICA-M1 lesions were treated in 3 patients and 2 patients had only M1 stenoses treated. One patient underwent angioplasty alone of an ICA-M1 lesion. The remainder of the procedures were angioplasty with Wingspan stent placement. In 2 of the 5 patients the angiopathy was bilateral. One patient with bilateral disease had treatment of both ICAs. Another with bilateral

Time to recurrent endovascular treatment months	Recurring symptoms in territory of endovascular treatment	Angiographic findings prior to surgical treatment	Surgery	Clinical follow-up after surgical revascularization
3	yes/TIAs	70% instent stenosis – 6 months after initial endovascular treatment	right STA-MCA bypass – 9 months after last endovascular treatment	asymptomatic, no new strokes 15 months after bilateral STA-MCA bypass
4	yes/TIAs	70% instent stenosis – 6 months after initial endovascular treatment	left STA-MCA bypass – 8 months after last endovascular treatment	
	yes/TIAs	new left PCA stenosis and left M1 occlusion – 2 months after initial endovascular treatment	left STA-MCA bypass – 14 months after last endovascular treatment	asymptomatic, no new strokes 28 months after left STA-MCA bypass
	yes/TIAs	90% instent stenosis – 3 months after initial endovascular treatment, additional irregularity of the M1	left STA-MCA bypass – 6 months after last endovascular treatment (also right STA-MCA bypass at 6 months)	asymptomatic, no new strokes 22 months after bilateral STA-MCA bypass
2	yes/TIAs	mild instent stenosis, 50% stenosis proximal to stent, 70% stenosis distal to stent – 9 months after initial endovascular treatment	left STA-MCA bypass – 3 months after last endovascular treatment	asymptomatic, no new strokes 11 months after left STA-MCA bypass
7				
6	yes/TIAs	near occlusion of M1 – 13 months after initial endovascular treatment	left STA-MCA bypass – 5 months after last endovascular treatment	asymptomatic, no new strokes 14 months after left STA-MCA bypass
8				

disease had 1 ICA treated while the other was already occluded. Moyamoya vessels were present in all patients. All patients presented with repeated transient ischemic attacks (TIAs) in the vascular territory of endovascular treatment after their initial therapy. All patients showed restenosis in the angioplasty and stented segments (table 1).

Repeat endovascular treatment was performed within an average of 3 months (0–6 months) in 3 patients (4 lesions). Two of these patients (2 lesions) remained clinically symptomatic despite repeat endovascular treatment so that a third endovascular treatment was performed. Angiographically one of these patients had a 50% instent stenosis at the proximal end of the stent and a 70% stenosis distal to the stent. In the other patient there was near occlusion of the M1.

All patients were symptomatic when referred to our institution after their final endovascular therapeutic procedure. Follow-up angiography at the time of consulta-

tion in our clinic demonstrated 70–90% instent restenosis of the stented vessel in 4 patients (5 lesions) and occlusion in 1 patient. Due to persistence of symptoms along with the progression of stenosis in the endovascularly treated vessels, cerebral revascularization was indicated and performed in all patients.

All patients underwent unilateral superficial temporal artery to middle temporal artery (STA-MCA) bypass in the affected hemisphere. Bilateral cerebral revascularization (STA-MCA bypass) was performed in 2 patients. All patients were asymptomatic without any further TIAs at a mean follow-up of 18 months (range = 11–28).

Two Illustrative Cases

Case 1

A 37-year-old right-handed female presented with left hemisphere TIAs manifest as right body numbness, weakness and speech difficulties. She was initially treated with clopidogrel bisulfate (Plavix) and aspirin. Angiography

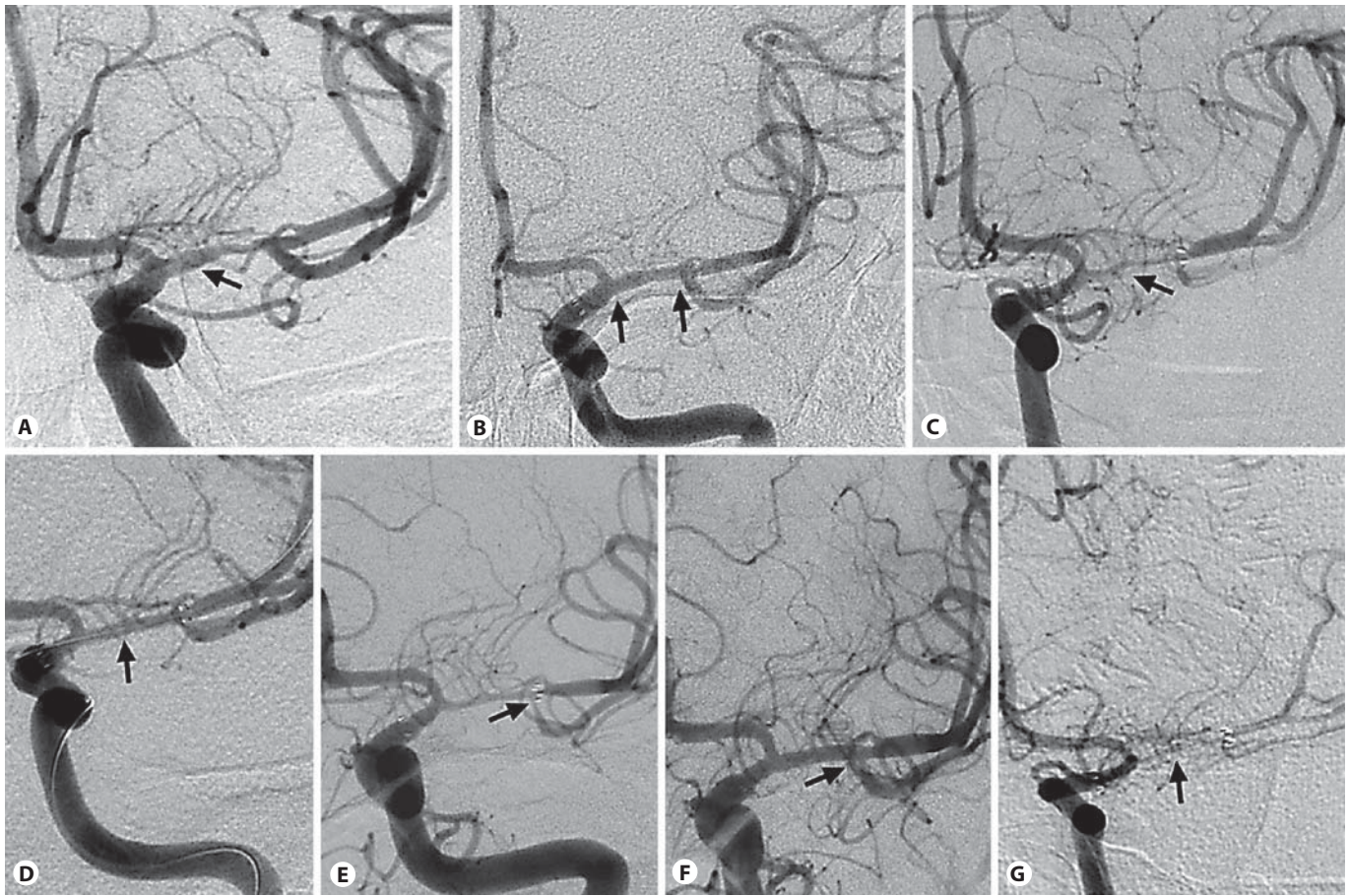


Fig. 1. **A** Anteroposterior angiograms of the left ICA. Initial M1 stenosis (arrow). **B** Angioplasty and stenting showing increased M1 diameter (arrows). **C** Recurrence of stenosis at 6 months (arrow). **D** Reangioplasty at 6 months. **E** Repeat angiography 2 months later reveals recurrent high-grade M1 and proximal M2 stenoses (arrow). **F** Reangioplasty of both M1 and M2 (arrow). **G** Occlusion of M1 segment prior to revascularization surgery (arrow).

showed a 70% left M1 stenosis (with some moyamoya vessels) for which she underwent stenting. Recurrence of symptoms and progression of the M1 stenosis was noted at 6 months of follow-up and M1 angioplasty was performed. There was no improvement of her symptomatology and repeat angiography at 2 months revealed a preocclusive high-grade M1 stenosis, as well as stenosis of the proximal M2 segment. She was still on clopidogrel bisulfate (Plavix) and aspirin at the time of recurrence of symptoms. Reangioplasty of both the M1 and M2 segments was performed again without improvement of symptoms. Angiographic follow-up at 5 months showed near complete occlusion of the M1 segment (fig. 1). Due to persistence of symptoms and complete M1 occlusion, a left STA-MCA bypass was performed. She has remained asymptomatic for 14 months since her revascularization surgery.

Case 2

A 19-year-old left-handed female with MMD presented at an outside hospital with bihemispheric TIAs with slurred speech and transient sensory disturbances of her left arm and leg. Angiography showed right ICA occlusion and a >70% stenosis of the supraclinoid ICA on the left (with some moyamoya vessels). Treatment of the left ICA stenosis was recommended at the outside hospital. She therefore underwent left ICA percutaneous balloon angioplasty and Wingspan stent, which reduced the stenosis to 30%. She was also placed on aspirin and clopidogrel bisulfate (Plavix). She initially improved, however, her TIAs recurred at 3 months when a follow-up angiography showed severe restenosis of the left ICA as well as mild narrowing and irregularity of the M1 segment (fig. 2). Due to bilateral disease and recurrence of symp-

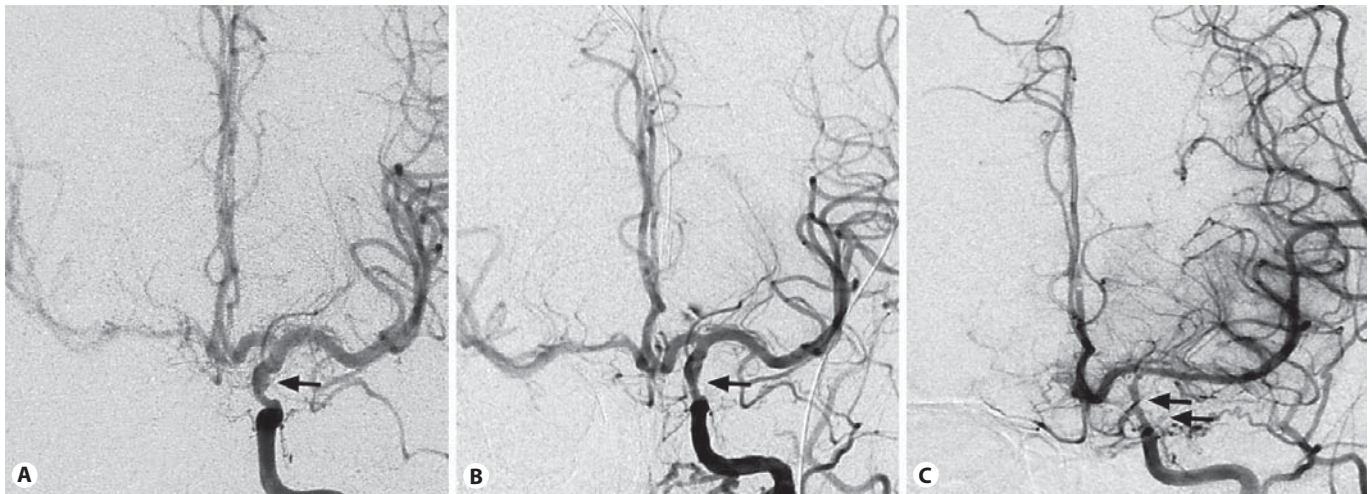


Fig. 2. Anteroposterior angiograms of the left ICA demonstrating >70% stenosis of the supraclinoid ICA (**A**, arrow) and 30% residual stenosis after stenting (**B**, arrow). **C** Progression to 90% in-stent stenosis at 6 months of follow-up (arrows).

toms similar to those prior to her initial endovascular treatment, bilateral STA-MCA revascularization was performed. Her postoperative course has been uneventful at 22 months of follow-up with no recurrent TIAs.

Discussion

MMD is often a bilateral and multifocal angiopathy with progression of stenosis/occlusion along the entire circle of Willis observed commonly in children and young adults [9–11]. The majority of patients present with bilateral symptomatic disease and with impairment in cerebral perfusion reserves in both hemispheres. Treatment should therefore aim at alleviating symptoms, preventing stroke in both cerebral hemispheres, and the results should be durable. Percutaneous balloon angioplasty and/or stenting is appealing as a less invasive treatment method to achieve immediate increase in cerebral blood flow with a shorter hospitalization time in comparison to microsurgical revascularization.

There is, however, little documented experience with endovascular therapy of MMD. Only 4 previous single case reports of MMD angiopathy treated percutaneously with balloon angioplasty with or without stenting have been described in the literature. Centers may not choose to report their limited experience, particularly if the procedure is not successful. Rodriguez et al. [8] described a 37-year-old patient with bilateral ICA stenoses presenting

with left hemisphere TIAs, where angioplasty of the distal left ICA and MCA was performed to successfully increase flow. Two-year angiographic follow-up revealed decrease in the moyamoya collaterals without evidence of restenosis and no recurrence of TIAs. The second case in the literature [7] was an 18-year-old female patient with essential thrombocythemia and left hemispheric TIAs. Angiography confirmed bilateral MMD involving the supraclinoid ICAs and additional involvement of the left M1 segment. A stent was placed in the left intracranial ICA with resolution of her TIAs. No restenosis was observed at 46 months. The third case was that of a Caucasian MMD twin who underwent angioplasty of a left MCA stenosis and Wingspan stenting of a right ICA stenosis [5]. The left MCA thrombosed on discontinuation of clopidogrel bisulfate and the Wingspan stent underwent in-stent restenosis requiring repeat angioplasty. However, the authors report a 15-month stroke-free interval after the last endovascular treatment.

A recent fourth case of a 3-year-old girl with moyamoya syndrome has been reported [6]. After developing acute left hemiplegia she underwent balloon angioplasty of a nearly occluded right supraclinoid ICA within 6 h of symptom onset with rapid improvement of motor function and angiographical improvement in the luminal diameter of the right ICA.

Recognition of the distinct angiographical features of MM angiopathy versus atherosclerosis is crucial for correct management, as both have similar clinical presenta-

tions but different mechanisms causing intraluminal stenoses/occlusion.

Previous literature on angioplasty alone for symptomatic intracranial atherosclerotic stenosis has shown a high rate of technical success with a low rate of subsequent stroke [12, 13]. Reports with the Wingspan stent have shown this treatment strategy to have relatively higher rates of restenosis for symptomatic intracranial atherosclerotic stenoses affecting particularly the supraclinoid ICA in young patients. These reports suggest that these lesions might be of a different nature than the typical primary atherosclerotic lesions observed in older patients, that is, they may be of inflammatory origin or may simply represent MMD angiopathy [14–16].

Restenoses within a previously angioplastied or stented segment in all the cases in this reported series may reflect a different response in the vessel wall in MMD and could be the result of natural progression of disease that is characteristic for MMD. Two of our 5 patients showed progression of disease unrelated to the site of the angioplasty or stent placement (1 in the posterior cerebral artery and the other in the left M1 prior to cerebral revascularization).

Surgical revascularization for MMD is safe and effective in the hands of an experienced surgeon, and results in long-term cerebral blood flow augmentation and durable prevention against future TIAs and stroke. The efficacy of microsurgical revascularization (STA-MCA bypass and/or indirect revascularization) for stroke prevention in MMD has been extensively detailed in the literature [2, 17–22]. All patients in this series were asymptomatic at an average follow-up of 18 months after

surgery. The limitations of our series include the small number of patients initially treated with angioplasty/stenting, a potential referral bias to Stanford for MMD patients who failed angioplasty/stenting and the relatively short follow-up for outcome after revascularization surgery.

Conclusion

Percutaneous balloon angioplasty and/or stenting may be an attractive, less invasive treatment to achieve immediate increase in cerebral blood flow with a shorter hospitalization time in comparison to microsurgical revascularization. However, in our small series the recurrence of clinical symptoms and evidence of restenosis and/or occlusion in previously angioplastied and/or stented vessels with an average period of 1.8 months and 3.9 months, respectively, provides evidence that endovascular treatment is not durable and may not provide long-term prevention against future ischemic events in MMD.

Acknowledgements and Disclosure

The authors have no conflict of interest to declare. This work was supported in part by Russell and Elizabeth Siegelman, Bernard and Ronni Lacroute, the William Randolph Hearst Foundation, Stanley and Alexis Shin, and the Huber Family Moyamoya Fund.

We thank Cindy H. Samos for assistance with the manuscript and Beth Hoyte for preparation of the figures.

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